

**Different Conbercept Injection
Methods in Treatment of Severe
Proliferative Diabetic Retinopathy**

NCT02816710

2016-06-30

Study Protocol

1. Study objectives:

To evaluate the clinical efficacy of preoperative, intraoperative or preoperative combined with intraoperative intravitreal conbercept (IVC) in vitrectomy with silicone oil tamponade for severe PDR patients.

2. Study design:

This is a prospective, open-labelled, randomized controlled trial to assess the clinical efficacy of preoperative, intraoperative or preoperative combined with intraoperative IVC injection in pars plana vitrectomy (PPV) with silicone oil tamponade for patients with severe proliferative diabetic retinopathy (PDR). The study was registered on 25 June 2016 (as NCT02816710).

3. Participants:

2.1 inclusion criteria:

1. Subjects of either sex aged ≥ 18 years.
2. Diagnosis of diabetes mellitus (type 1 or type 2);
3. Active proliferative diabetic retinopathy was clinically evident;
4. Study eyes required a vitrectomy and silicone oil tamponade due to vitreous hemorrhage with significant fibrous proliferation, tractional retinal detachment in the posterior pole or complicated retinal detachment, which can be detected by B-scan ultrasonography.
5. Ability to give informed consent.

2.2 exclusion criteria:

1. Coexistent ocular disease that may interfere with visual outcome;
2. Prior vitreoretinal surgery or anti-VEGF pharmacotherapy in either eye;
3. A macula-involving retinal detachment for >6 months in the study eye;
4. Iris or angle neovascularization and neovascular glaucoma;

5. known allergy to any components of conbercept formulation
6. severe external ocular infection;
7. pregnancy or current oral contraceptive intake;
8. usage of anticoagulant or antiplatelet therapy;
9. preoperative or postoperative poor diabetes control [serum hemoglobin A1c (HbA1c) >11.0%];
10. uncontrolled systemic diseases, such as hypertension, cardiac diseases or presenting abnormal coagulation-associated blood diseases;
11. <6 months of follow-up post initial surgery.

4. Randomization:

Patients were recruited at the department of Ophthalmology, Ruijin Hospital, affiliated with Shanghai Jiaotong University School of Medicine, between July 2016 and September 2017, after approval of the local ethics committee. The use of conbercepts were discussed with patients, who all gave their written informed consent to undergo the procedure, after having been provided with a detailed description of the treatment. Eligible subjects after enrollment were randomized into one of the three possible treatment groups. Randomization was performed by an automated system at a 1: 1:1 ratio to 1 of 3 treatment arms: Group A received IVC (0.5 mg/0.05 mL) 3–5 days before PPV, while Group B received IVC (0.5mg/0.05 mL) at the end of PPV. Group C received an IVC injection 3 to 5 days before PPV as well as an IVC injection at the end of operation.

5. Interventions:

Injections were administered according to the product recommendations and different time points under controlled aseptic conditions using sterile gloves, a sterile drape and a sterile eyelid speculum. Adequate topical anesthesia together with a broad-spectrum microbicide were administered prior to injection. All patients underwent 23-gauge transconjunctival suture-less vitrectomy using a 23-gauge trocar and cannula system. Simultaneously, phacoemulsification and aspiration (PEA) were performed in patients with cataracts, and an acrylic foldable intraocular lens (IOL) was placed in the capsular bag. During the operation,

hemostasis was maintained by endodiathermy. After vitrectomy, the vitreous body, preretinal fibrovascular tissue and tractional membranes were removed using a combination of segmentation and delamination techniques. If subretinal fibrotic bands were present, these bands were removed through retinotomy with subretinal forceps. The surgical endpoint was relief of traction on the macula and neovascular fronds that allowed the entire retinal to flatten, with silicone oil tamponade subsequently.

6. Assessments:

Included patients were followed at 1 day, 1 week, 1 month, 3 months, and 6 months after the operation. At baseline, the measurements included: a complete ophthalmological examination, with BCVA evaluated using logMAR visual acuity measurement, intraocular pressure (IOP), previous history of PRP, lens status, preoperative iris neovascularization, surgical indications. During surgery, the extent of vitreoretinal adhesion, degree of intraoperative bleeding, frequency of electrocoagulation, surgery duration and combined lens extraction were recorded carefully. At each time point during postoperative follow-up, incidence of recurrent VH, preretinal blood absorption time, BCVA, IOP, rubeosis, NVG, TRD, reoperation rate and systemic adverse events were evaluated respectively.